

Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (Currently Amended) A method of evaluating a compound, the method comprising contacting a Silent Information Regulator (SIR) polypeptide having ~~acetylase or~~ deacetylase activity, ~~or fragment thereof~~, with a compound, in the presence of a cytochrome c polypeptide, wherein the amino acid sequence of the SIR polypeptide comprises an amino acid sequence that is at least 95% identical to an amino acid sequence of a SIR protein selected from the group consisting of: SIRT1 (SEQ ID NO:1); SIRT2 (SEQ ID NO:2); SIRT3 (SEQ ID NO:3); SIRT4 (SEQ ID NO:4); SIRT5 (SEQ ID NO:5); SIRT6 (SEQ ID NO:6); and SIRT7 (SEQ ID NO:7), and

evaluating if the compound modulates interaction between the SIR polypeptide and the cytochrome c polypeptide.

2. (Original) The method of claim 1, wherein the cytochrome c polypeptide is acetylated at at least one lysine.

3. (Currently Amended) The method of claim 1, wherein the cytochrome c polypeptide is full length cytochrome c polypeptide.

4. (Currently Amended) The method of claim 1, wherein the cytochrome c polypeptide is human cytochrome c polypeptide.

5. (Currently Amended) The method of claim 1, wherein the cytochrome c polypeptide is a fragment of between 3 and 20 amino acids of a full length cytochrome c polypeptide.

6. – 7. (Canceled)

8. (Currently Amended) The method of claim 1 ~~claim 7~~, wherein the SIR polypeptide is SIRT1 (SEQ ID NO:1), SIRT2 (SEQ ID NO:2), or SIRT3 (SEQ ID NO:3).

9. (Currently Amended) A method comprising:
contacting a cell which expresses a SIR polypeptide having ~~deacetylase~~ ~~acetylation or deacetylation~~ activity and a cytochrome c polypeptide with a test compound, wherein the amino acid sequence of the SIR polypeptide comprises an amino acid sequence that is at least 95% identical to an amino acid sequence of a SIR protein selected from the group consisting of: SIRT1 (SEQ ID NO:1); SIRT2 (SEQ ID NO:2); SIRT3 (SEQ ID NO:3); SIRT4 (SEQ ID NO:4); SIRT5 (SEQ ID NO:5); SIRT6 (SEQ ID NO:6); and SIRT7 (SEQ ID NO:7), and
determining if the test compound modulates acetylation of the cytochrome c polypeptide.

10. (Original) The method of claim 9 further comprising evaluating apoptosis or an indication of apoptosis in the cell.

11. (Currently Amended) A method of evaluating a test compound, the method comprising:
contacting a SIR polypeptide having ~~acetylase or deacetylase activity, or fragment thereof,~~ with a test compound, in the presence of a cytochrome c polypeptide, in vitro, wherein the amino acid sequence of the SIR polypeptide comprises an amino acid sequence that is at least 95% identical to an amino acid sequence of a SIR protein selected from the group consisting of: SIRT1 (SEQ ID NO:1); SIRT2 (SEQ ID NO:2); SIRT3 (SEQ ID NO:3); SIRT4 (SEQ ID NO:4); SIRT5 (SEQ ID NO:5); SIRT6 (SEQ ID NO:6); and SIRT7 (SEQ ID NO:7), and
evaluating if the test compound modulates interaction between the SIR polypeptide and the cytochrome c polypeptide;
contacting a cell which expresses ~~[[a]]~~ the SIR polypeptide ~~having acetylation or deacetylation activity~~ and a cytochrome c polypeptide with the test compound, and
determining if the test compound modulates acetylation of the cytochrome c polypeptide in the cell.

12. – 21. (Canceled)

22. (New) The method of claim 1, wherein the SIR polypeptide comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SIRT1 (SEQ ID NO:1).

23. (New) The method of claim 22, wherein the SIR polypeptide comprises the amino acid sequence of SIRT1 (SEQ ID NO:1).

24. (New) A method of evaluating a compound, the method comprising contacting a Silent Information Regulator (SIR) polypeptide having deacetylase activity with a compound, in the presence of a cytochrome c polypeptide, wherein the SIR polypeptide comprises an amino acid sequence that is encoded by a nucleic acid that hybridizes under high stringency conditions (hybridizes in 6X SSC at about 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 65°C) to the complement of a nucleic acid encoding an amino acid sequence of a SIR protein selected from the group consisting of: SIRT1 (SEQ ID NO:1); SIRT2 (SEQ ID NO:2); SIRT3 (SEQ ID NO:3); SIRT4 (SEQ ID NO:4); SIRT5 (SEQ ID NO:5); SIRT6 (SEQ ID NO:6); and SIRT7 (SEQ ID NO:7), and evaluating if the compound modulates interaction between the SIR polypeptide and the cytochrome c polypeptide.

25. (New) The method of claim 24, wherein the SIR polypeptide comprises an amino acid sequence that is encoded by a nucleic acid that hybridizes under high stringency conditions (hybridizes in 6X SSC at about 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 65°C) to a nucleic acid encoding the amino acid sequence of SIRT1 (SEQ ID NO:1).

26. (New) The method of claim 24, wherein nicotinamide adenine dinucleotide (NAD) or an NAD analog is present during the contacting step.

27. (New) The method of claim 1, wherein NAD or an NAD analog is present during the contacting step.

28. (New) The method of claim 9, wherein NAD or an NAD analog is present during the contacting step.

29. (New) A method comprising:

contacting a cell which expresses a SIR polypeptide having deacetylase activity and a cytochrome c polypeptide with a test compound, wherein the SIR polypeptide comprises an amino acid sequence that is encoded by a nucleic acid that hybridizes under high stringency conditions (hybridizes in 6X SSC at about 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 65°C) to the complement of a nucleic acid encoding an amino acid sequence of a SIR protein selected from the group consisting of: SIRT1 (SEQ ID NO:1); SIRT2 (SEQ ID NO:2); SIRT3 (SEQ ID NO:3); SIRT4 (SEQ ID NO:4); SIRT5 (SEQ ID NO:5); SIRT6 (SEQ ID NO:6); and SIRT7 (SEQ ID NO:7), and

determining if the test compound modulates acetylation of the cytochrome c polypeptide.

30. (New) The method of claim 29, wherein NAD or an NAD analog is present during the contacting step.

31. (New) The method of claim 11, wherein NAD or an NAD analog is present during the contacting step.

32. (New) A method of evaluating a test compound, the method comprising:

contacting a SIR polypeptide having deacetylase activity with a test compound in the presence of a cytochrome c polypeptide, in vitro, wherein the SIR polypeptide has deacetylase activity and wherein the SIR polypeptide comprises an amino acid sequence that is encoded by a nucleic acid that hybridizes under high stringency conditions (hybridizes in 6X SSC at about 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 65°C) to the complement of a nucleic acid encoding an amino acid sequence of a SIR protein selected from the group

consisting of: SIRT1 (SEQ ID NO:1); SIRT2 (SEQ ID NO:2); SIRT3 (SEQ ID NO:3); SIRT4 (SEQ ID NO:4); SIRT5 (SEQ ID NO:5); SIRT6 (SEQ ID NO:6); and SIRT7 (SEQ ID NO:7), and

evaluating if the test compound modulates interaction between the SIR polypeptide and the cytochrome c,

contacting a cell which expresses the SIR polypeptide and a cytochrome c polypeptide with the test compound, and

determining if the test compound modulates acetylation of the cytochrome c polypeptide in the cell.

33. (New) The method of claim 32, wherein NAD or an NAD analog is present during the contacting step.